Supporting Information

Catalyst-Free Synthesis of Spiropyrazolines from Chalcones and Cyclic-Ketone N-Tosylhydrazones

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2. General Information

Common reagents and materials were purchased from commercial sources and purified by recrystallization or distillation. Where necessary, organic solvents were routinely dried and/or distilled prior to use and stored over molecular sieves under argon. Organic extracts were, in general, dried over anhydrous sodium sulfate (Na₂SO₄). TLC plates were visualized by exposure to ultraviolet light (UV). Chemical shifts for protons are reported in parts per million (δ scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvents (CHCl₃: δ 7.26). Chemical shifts for carbon resonances are reported in parts per million (δ scale) downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent (CDCl₃: δ 77.0). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant in Hertz (Hz), and integration.
3. Experimental Procedure

A mixture of a ketone (4a–k, 0.2 mmol) and tosylhydrazide (0.2 mmol) in methanol (MeOH, 1 mL) was stirred at room temperature for 3 hours, then solvent was removed in vacuo to give a ketone N-tosylhydrazone (2a–k, 0.2 mmol). Subsequently, the mixture of the resulting ketone N-tosylhydrazone (2a–k, 0.2 mmol), Cs₂CO₃ (0.2 mmol) and a chalcone (1a–e, 0.1 mmol) in MeCN (1.0 mL) was stirred at 110 °C (screw-capped vial) for 2 hours under argon, cooled to room temperature, and added with water (10 mL) and ethyl acetate (10 mL). The two layers were separated, and the aqueous phase was extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were washed by brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by flash chromatography on silica gel (100–200 mesh) to afford the desired spiropyrazoline (3a–o).

![Chemical Structure](image)

Spiropyrazoline 3a: Pale yellow solid; m.p. = 180–181 °C; 'H NMR (400 MHz, CDCl₃) δ 8.10 (d, J = 7.3 Hz, 2H), 7.52–7.05 (m, 9H), 4.24 (s, 1H), 1.72–1.24 (m, 10H); '³C NMR (100 MHz, CDCl₃) δ 187.5, 153.1, 137.5, 136.1, 132.1, 129.9, 128.6, 128.4, 127.9, 127.1, 67.1, 57.7, 37.3, 31.6, 25.2, 23.4, 22.4; FTIR (film): 3315, 2930, 2855, 1625, 1449, 1423, 1226, 870, 718, 699 cm⁻¹. HRMS (ESI) m/z: Calcd for C₂₁H₂₂N₂NaO [M+Na]⁺: 341.1624. Found: 341.1619.

Spiropyrazoline 3b: Pale yellow solid; m.p. = 174–175 °C; 'H NMR (400 MHz, CDCl₃) δ 8.13 (d, J = 7.4 Hz, 2H), 7.54–7.07 (m, 8H), 6.77 (s, br, 1H), 4.16 (s, 1H), 2.03–1.03 (m, 9H), 0.90 (d, J = 5.8 Hz, 3H); '³C NMR (100 MHz, CDCl₃) δ 187.6, 152.9, 137.5, 136.2, 132.1, 129.9, 128.4, 128.3, 127.9, 127.1, 68.7, 59.2, 37.3, 31.8 (d), 31.4, 31.1, 22.0; FTIR (film): 33327, 2949, 2924, 2867, 1708, 1673, 1624, 1598, 1449, 1422, 1221, 857, 717, 699 cm⁻¹. HRMS (ESI) m/z: Calcd for C₂₂H₂₅N₂ [M+H]⁺: 333.1961. Found: 333.1960.
Spiropyrazoline 3c: Pale yellow solid; m.p. = 169–170 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 8.19 (d, $J = 6.3$ Hz, 2H), 7.56–7.13 (m, 8H), 5.99 (s, br, 1H), 4.21 (s, 1H), 2.06–0.87 (m, 14H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 187.4, 152.7, 137.4, 136.1, 132.0, 129.9, 128.5, 128.3, 127.9, 127.0, 69.0, 59.2, 38.0, 31.7, 29.3, 29.1, 28.6, 11.3; FTIR (film): 3306, 2956, 2924, 2856, 1610, 1574, 1531, 1447, 1425, 1219, 860, 717, 698 cm$^{-1}$. HRMS (ESI) m/z: Calcd for C$_{23}$H$_{27}$N$_2$O [M+H]$^+$: 347.2118. Found: 347.2149.

Spiropyrazoline 3d: Pale yellow solid; m.p. = 163–164 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 8.15 (d, $J = 7.1$ Hz, 2H), 7.55–7.07 (m, 8H), 5.65 (s, br, 1H), 4.16 (s, 1H), 2.10–0.90 (m, 9H), 0.84 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 187.4, 152.8, 137.4, 136.1, 132.0, 129.9, 128.3, 128.2, 127.9, 127.0, 68.7, 59.4, 46.9, 38.0, 32.5, 27.3, 24.0, 23.4; FTIR (film): 3313, 2948, 2866, 1611, 1447, 1426, 1223, 1120, 860, 697 cm$^{-1}$. HRMS (ESI) m/z: Calcd for C$_{25}$H$_{31}$N$_2$O [M+H]$^+$: 375.2431. Found: 375.2437.

Spiropyrazoline 3e: Pale yellow solid; m.p. = 153–154 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 8.11 (d, $J = 6.6$ Hz, 2H), 7.54–7.05 (m, 8H), 6.08 (s, br, 1H), 4.16 (s, 1H), 3.72 (s, br, 1H), 2.06–1.13 (m, 12H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 187.5, 169.8, 1152.2, 137.4, 135.8, 132.2, 129.8, 128.5, 128.2, 128.0, 127.3, 68.0, 58.6, 47.1, 35.7, 30.3, 29.0, 28.3, 23.1; FTIR (film): 3286, 2928, 2854, 1629, 1539, 1471, 1448, 1431, 1369, 1221, 1143, 1125, 860, 719, 700 cm$^{-1}$. HRMS (ESI) m/z: Calcd for C$_{23}$H$_{26}$N$_3$O$_2$ [M+H]$^+$: 376.2020. Found: 375.2015.

Spiropyrazoline 3f: White solid; m.p. = 185–186 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 8.13 (d, $J = 7.3$ Hz, 2H), 7.56–7.16 (m, 8H), 6.59 (s, br, 1H), 4.37 (s, 1H), 3.83 (dd, $J = 28.5, 4.1$ Hz, 2H), 3.54 (s, 2H), 1.88–1.42 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 187.3, 153.3, 137.2, 135.2, 132.4, 129.9, 128.7, 128.6, 128.0, 127.5, 66.9, 65.5, 64.0, 57.2, 37.6, 31.7; FTIR (film): 3300, 2957, 2924, 2852, 1626, 1575, 1535, 1448, 1429, 1384, 1225, 1105, 861, 718, 700 cm$^{-1}$. HRMS (ESI) m/z: Calcd for C$_{20}$H$_{21}$N$_2$O$_2$ [M+H]$^+$: 321.1598. Found: 321.1596.
Spiropyrazoline 3g: Yellow solid; m.p. = 155–156 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.12 (d, \(J = 7.3\) Hz, 2H), 7.53–7.11 (m, 8H), 6.78 (s, br, 1H), 4.28 (s, 1H), 2.67–2.18 (m, 7H), 1.87–1.44 (m, 4H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 187.3, 152.9, 137.3, 135.5, 132.2, 129.9 (d), 128.5, 127.9, 127.3, 66.9, 53.0, 51.8, 45.8, 36.7, 31.0, 29.6; FTIR (film): 3304, 2924, 2853, 1625, 1449, 1431, 1378, 1226, 1131, 860, 718, 699 cm\(^{-1}\). HRMS (ESI) m/z: Calcd for C\(_{21}\)H\(_{25}\)N\(_3\)O \([M+H]^+: 334.1914. Found: 334.1916.

Spiropyrazoline 3h: Yellow foam; m.p. = 67–68 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.11 (d, \(J = 7.6\) Hz, 2H), 7.52–7.11 (m, 9H), 4.31 (s, 1H), 3.64–3.18 (m, 4H), 1.74–1.33 (m, 13H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 187.2, 154.5, 152.6, 137.2, 135.3, 132.2, 129.8, 128.6, 128.4, 127.9, 127.4, 79.8, 67.7, 56.9, 41.0, 39.7, 36.3, 30.9, 28.3; FTIR (film): 3300, 1692, 1671, 1630, 1449, 1422, 1366, 1265, 1247, 1164, 860, 700 cm\(^{-1}\). HRMS (ESI) m/z: Calcd for C\(_{25}\)H\(_{30}\)N\(_3\)O\(_3\) \([M+H]^+: 420.2282. Found: 420.2283.

Spiropyrazoline 3i: Yellow foam; m.p. = 61–62 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.14 (d, \(J = 8.6\) Hz, 2H), 7.57–7.14 (m, 13H), 6.70 (s, br, 1H), 4.32 (s, 1H), 2.86–1.52 (m, 12H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 187.3, 153.1, 139.7, 137.3, 135.5, 132.3, 129.9, 128.8, 128.6, 128.4, 128.3, 128.0, 127.4, 126.2, 67.4, 60.1, 57.2, 51.0, 49.8, 36.6, 33.4, 30.9; FTIR (film): 3309, 2926, 1624, 1575, 1536, 1494, 1449, 1428, 1375, 1225, 1128, 860, 749, 718, 699 cm\(^{-1}\). HRMS (ESI) m/z: Calcd for C\(_{28}\)H\(_{30}\)N\(_3\)O \([M+H]^+: 424.2383. Found: 424.2389.

Spiropyrazoline 3j: Yellow solid; m.p. = 141–142 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.11 (d, \(J = 7.8\) Hz, 2H), 7.52–7.12 (m, 8H), 6.48 (s, br, 1H), 4.24 (s, 1H), 1.91–1.37 (m, 8H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 187.3, 152.9, 137.6, 137.5, 132.1, 129.9, 128.6, 128.0, 127.9, 127.1, 78.5, 57.2, 41.0, 31.7, 22.9, 22.7; FTIR (film): 3304, 2957, 2873, 1673, 1598, 1575, 1526, 1494, 1448, 1423, 1229, 1156, 717, 699 cm\(^{-1}\). HRMS (ESI) m/z: Calcd for C\(_{20}\)H\(_{24}\)N\(_3\)O \([M+H]^+: 305.1648. Found: 305.1648.
Spiropyrazoline 3k: Yellow foam; m.p. = 59–60 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 8.10 (d, $J = 7.6$ Hz, 2H), 7.54–7.01 (m, 12H), 6.68 (s, br, 1H), 4.27 (s, 1H), 2.83–2.38 (m, 8H), 2.29 (s, 3H), 1.91–1.54 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 187.4, 153.2, 139.6, 137.3, 137.0, 132.4, 132.2, 129.9, 129.4, 128.6, 128.4 (d), 128.0, 126.2, 67.2, 60.1, 56.8, 51.0, 49.8, 36.5, 33.3, 30.8, 21.0; FTIR (film): 3309, 2924, 2810, 1624, 1575, 1536, 1513, 1449, 1428, 1375, 1226, 1180, 1127, 861, 727, 699 cm$^{-1}$. HRMS (ESI) m/z: Calcd for C$_{29}$H$_{32}$N$_3$O $[M+H]^{+}$: 438.2540. Found: 438.2535.

Spiropyrazoline 3l: Yellow foam; m.p. = 64–65 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 8.10 (d, $J = 8.1$ Hz, 2H), 7.42–7.04 (m, 11H), 6.78 (s, br, 1H), 4.25 (s, 1H), 2.84–2.36 (m, 8H), 1.89–1.51 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 185.6, 152.4, 139.7, 138.8, 135.3, 134.1, 133.3, 131.4, 129.8, 128.9, 128.6, 128.4, 128.3, 126.2, 67.5, 60.1, 56.5, 50.9, 49.7, 36.6, 33.5, 30.9; FTIR (film): 3312, 2927, 1619, 1587, 1490, 1430, 1223, 1127, 1107, 1090, 1015, 861, 750, 699 cm$^{-1}$. HRMS (ESI) m/z: Calcd for C$_{28}$H$_{28}$Cl$_2$N$_3$O $[M+H]^{+}$: 492.1604. Found: 492.1608.

Spiropyrazoline 3m: Pale yellow liquid; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.25–7.09 (m, 5H), 6.46 (s, br, 1H), 2.86–1.14 (m, 25H), 8.10 (t, $J = 7.0$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 194.8, 154.1, 139.8, 128.6, 128.4, 128.1, 67.4, 60.1, 51.1, 49.8, 41.1, 35.7, 33.4, 31.5, 29.64, 29.59, 26.9, 26.4, 25.5, 22.6, 14.0; FTIR (film): 3291, 2928, 2856, 1714, 1659, 1541, 1497, 1454, , 1434, 1377, 1346, 1181, 1128, 1030, 946, 749, 700 cm$^{-1}$. HRMS (ESI) m/z: Calcd for C$_{23}$H$_{36}$N$_3$O $[M+H]^{+}$: 370.2854. Found: 370.2858.

Spiropyrazoline 3n: Pale yellow solid; m.p. = 157–158 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.32–7.04 (m, 10H), 6.56 (s, br, 1H), 4.07 (s, 1H), 2.86–2.31 (m, 11H), 1.88–1.44 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 193.8, 153.4, 139.8, 135.3, 128.7, 128.6, 128.5, 128.4,
127.3, 126.1, 68.0, 60.2, 56.1, 50.9, 49.8, 36.5, 33.5, 31.0, 25.5; FTIR (film): 3300, 2926, 2812, 1655, 1541, 1496, 1455, 1432, 1376, 1345, 1191, 1128, 1079, 889, 749, 701 cm\(^{-1}\). HRMS (ESI) m/z: Calcd for C\(_{23}\)H\(_{28}\)N\(_3\)O \([M+H]^+\): 362.2227. Found: 362.2220.

Pyrazoline 3o: Yellow solid; m.p. = 131–132 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\), 4:1 mixture of isomers, the major isomer was listed) \(\delta\) 8.15 (d, \(J = 6.0\) Hz, 2H), 7.55–7.12 (m, 8H), 5.60 (s, br, 1H), 4.47 (s, 1H), 1.91–0.70 (m, 10H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\), the major isomer was listed) \(\delta\) 187.1, 151.1, 137.7, 137.3, 131.9, 129.8, 128.5, 128.4, 127.9, 126.9, 72.8, 54.5, 36.8, 18.3, 17.0, 16.4; FTIR (film): 3304, 1608, 1575, 1527, 1455, 1423, 1390, 1229, 1143, 843, 700 cm\(^{-1}\). HRMS (ESI) m/z: Calcd for C\(_{20}\)H\(_{23}\)N\(_2\)O \([M+H]^+\): 307.1805. Found: 307.1816.
4. NMR Spectra of Spiropyrazolines 3a–o

Spiropyrazoline 3a

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
Spiropyrazoline 3b

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
Spiropyrazoline 3c

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
Spiropyrazoline 3d

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
Spiropyrazoline 3e

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
Spiropyrazoline 3f

$^1$H NMR (400 MHz, CDCl$_3$)

![NMR spectrum of Spiropyrazoline 3f](image)

$^{13}$C NMR (100 MHz, CDCl$_3$)

![NMR spectrum of Spiropyrazoline 3f](image)
Spiropyrazoline 3g

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
Spiropyrazoline 3h

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)

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Spiropyrazoline 3i

$^1$H NMR (400 MHz, CDCl₃)

$^{13}$C NMR (100 MHz, CDCl₃)
Spiropyrazoline 3j

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
Spiropyrazoline 3k

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
Spiropyrazoline 31

$^{1}$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
Spiropyrazoline 3m

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
Spiropyrazoline 3n

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
Pyrazoline 3o

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
Spiropyrazoline 3o

$^1$H/$^1$H COSY (300 MHz, CDCl$_3$)

$^1$H/$^1$H NOESY (500 MHz, CDCl$_3$)